EXAMPLE 7

FIG. 4 illustrates the results of analyses of apparent blood viscosity as a function of shear rate upon addition of dosage amounts of polysaccharide material to rat blood. Rats weighing approximately 0.25 kg were injected intravenously with a 1 mg. dose of the polysaccharide solution prepared according to Example 1. Shortly after administration blood was withdrawn from the inferior vena cava of experimental and control animals. Analyses were performed on a Brookfield microviscosimeter and Weissenberg rheogomiometer over shear rate ranges of 20–200 sec^{-1} and 500–20,000 sec^{-1}, respectively. The former ranges represent those commonly believed to be encountered in an animal vascular system. Some blood rheologists believe that ranges of shear rates approaching zero are important in vivo. Starting at the lowest shear rates measured, the apparent viscosity of blood from control rats fell rapidly from 7 cP to slightly under 3cP. The apparent viscosity of blood from rats administered the polysaccharide fell from an initial value of slightly more than 5 cP. to slightly under 4 cP. Furthermore, control blood became quasi-Newtonian at shear rates in excess of about 500 sec^{-1} while the experimental blood became quasi-Newtonian at a shear rate under 50 sec^{-1}. It is expected that at in vivo shear rates of from about 0 to about 200 sec^{-1}, substantial decreases in the viscosity of blood will occur upon addition of from about 1 to 100 mg/1 of polysaccharide.

It is proposed that the mechanism of action of the polysaccharide additives of the invention as cardiac output enhancers involves the unexpected diminution of blood viscosity by the polysaccharide additive. This is believed to be the first demonstration of such a phenomenon—inconsistent as it is with reported increases in blood viscosity upon addition of drag reducing agents such as polyethylene oxide. Because no similar effects have been obtained when the polysaccharide is added to water or plasma, it is speculated that the viscosity drop in blood is the result of erythrocytes becoming aligned among extended, electrically charged polysaccharide macromolecules. It is not difficult to envision various modes of operation of the polysaccharide in vivo. The molecules may, for example, increase axial flow in small vessels merely by being repelled from the negatively charged walls of the vessel or by interacting with positively charged fibrinogen molecules to diminish clumping of erythrocytes. According to these models, the relative linearity of the rhamnose, galactose and galacturonic acid polysaccharide macromolecule, its high molecular weight and its uniform negative electrical charge all contribute in some measure to cause unusually beneficial hemodynamic effects.

The absolute significance of each of the characteristics of linearity, high molecular weight and electrical charge has not been fully delineated but the relative significance of the characteristics in selection of a polysaccharide for practice of the invention is manifest. Apart from standard considerations of toxicity, ease of synthesis or purification and the like, it is not expected that low molecular weight, substantially branched and electrically neutral polysaccharides or other polymers will provide the benefits of the present invention. For example, preliminary screening of several naturally-occurring polymers, including guar, karaya and locust bean gums as well as DNA, reveals no enhancement of cardiac output.

In the above description of preferred modes of administration, reference is made to solutions of polysaccharide in physiological saline. Clearly, numerous other aqueous carrier or solvent systems may be employed without departing from the spirit of the invention. Thus, for example, the polymer may likely be administered in solution with plasma without diminishing the desired result of increasing cardiac output by factors in excess of those which may incidentally result from concurrent expansion of plasma volume and hemodilution.

The clearly preferred mode of providing the polysaccharide to the circulatory system is intravenous, including infusion and injection. The amounts of polysaccharide to be administered to a particular patient may be subject to variation depending upon such factors as body weight and the etiology and extent of tissue underperfusion (i.e., whether the patient treated is encountering cardiogenic shock, ischemia, or the like). It is contemplated that further developmental studies performed in a manner consistent with the above illustrative examples will reveal preferred dosage ranges generally in keeping with the finding that substantial enhancement of cardiac output in rats is provided by a 5 mg/kg dose of purified okra plant polysaccharide of Example 1.

On the basis of percent investigation it is expected that aqueous solutions of from about 1 to about 20 and perhaps as much as 100 or more milligrams of polysaccharide may be administered per kilogram of the patient's body weight and that such administration may be repeated from one to five times per day.

Numerous modifications and variations of our invention are expected to occur to those skilled in the art upon consideration of the above description. It is expected, for example, that decreases in blood viscosity attendant to administration of polysaccharide according to the invention may prove to be most beneficial in extracorporeal circulation of blood. Consequently only such limitations as appear in the appended claims should be placed thereon.

What is claimed is:

1. In the method for developing therapeutrically beneficial hemodynamic effects through administering polymers to the blood of patients, the improvement comprising enhancing the cardiac output of a patient in need of such enhancement and independently of volume expanding effect by administering a linear, high molecular weight, negatively-charged polysaccharide essentially consisting of rhamnose, galactose and galacturonic acid.

2. The method of claim **1** wherein the amount administered is from about 1 to about 100 milligrams of polysaccharide per kilogram of the patient's body weight.

3. A fluid for introduction into the circulatory system of a patient to increase cardiac output without substantial concurrent increse in circulatory volume, said fluid comprising an aqueous solution of from about 1 to about 100 mg/ml of a linear, high molecular weight, negatively charged polysaccharide consisting of rhamnose, galactose and galacturonic acid constituents in a relative ratio of about 10:27:25, respectively.

4. A fluid according to claim **3** wherein said aqueous solution further includes 0.85% by weight sodium chloride.

5. A fluid according to claim **3** wherein said polysaccharide is an extracted constituent of okra plant tissue.

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